Multiple Sclerosis (update)

Review questions

Evidence report	Type of review	Review questions	Outcomes
A	Editorial update	What are the key diagnostic criteria for the following: multiple sclerosis; probable multiple sclerosis; neuromyelitis optica and clinically isolated syndrome?	This question did not require an evidence review as it was aimed at updating recommendations from CG 186 to be in line with the 2017 update of the McDonald criteria.
B	Qualitative	What information, education and support do a) adults with clinically isolated syndrome b) adults with MS c) adults with MS receiving palliative care d) adults with MS who may become pregnant and their families and carers find most useful?	Themes will be derived from the evidence identified for this review and may include: • Preferred format of information provision (e.g. face-to-face discussion, remotely, paper, electronic, who gives the information) • Content of information (e.g., symptom reduction, timing of intervention) • Information sources other than healthcare professionals (e.g. support groups, online resources, telephone helpline, Apps) • The need for consistency in the information that is provided (especially when provided from more than one source) • Information needs for carers to be considered independently from the needs of the person they care for • Timing of information (timely, repeated when necessary, adapted to change in progression) • Decision making (sometimes being vague and euphemistic so that people with MS and their families and carers go away unable to plan • Greater understanding of own condition • Confidence in self-management • Impact of treatment on lifestyle and lifestyle on treatment • Impact on family • Impact on sexual function • Impact on cognition

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			• Psychological support (e.g., for support with anxiety, fear, confidence) • Delivery of support (e.g. patient's GP, specialist nurse, peer groups) • Speed of response from nurse, consultant etc. • Transition from relapsing remitting to progressive • Role of the MS nurse or health care professional central to coordination of care and their impact on patient experience • Information needs for adults with MS who may become pregnant
C	Intervention	For adults with MS, including people receiving palliative care, what is the clinical and cost effectiveness of interventions for spasticity?	• Spasticity scales for example: ○ Modified Ashworth scale ○ Tardieu Scale ○ Muscle Elastography MS Scale (MEMSs) ○ Fugl Meyer Scale (FMS) • Patient reported measures of spasticity for example: ○ Penn Spasm Frequency Scale ○ Numeric Rating Scale for Spasticity (NRS-S) ○ MS Spasticity Scale-88 (MSSS) ○ Patient-reported Impact of Spasticity Measure (PRISM) • Health-related Quality of Life, for example EQ-5D, SF-36, Leeds MS quality of life scale, MS Impact Scale • Adverse effects of treatment for example: ○ Any adverse events ○ Adverse events leading to withdrawal ○ Drowsiness ○ Weakness ○ Nausea ○ Mobility • Pain scales for example visual analogue scale (VAS)

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			• Improvement in sleep • Comfort and posture positioning (self reported) • Functional scales that quantify level of disability, such as the Expanded Disability Status Scale (EDSS), the Multiple Sclerosis Functional Composite (MSFC), the Cambridge Multiple Sclerosis Basic Score (CAMBS), the Functional Assessment of Multiple Sclerosis (FAMS), the National Fatigue Index (NFI) or the MS walking scale. • Impact on patients/ carers **Follow up:** • 3-6 months (minimum of 3 months but can include 1-3 months and downgrade) • >6 months – 1 year (data from >1 year follow up may be included but will be downgraded)
D	Intervention	For adults with MS, including people receiving palliative care, what is the clinical and cost effectiveness of interventions for pain?	• Pain intensity using validated pain scales for example Visual Analogue Scale and numerical rating scale • Pain reduction for example >30% and 50% pain reduction from baseline • Patient-reported outcome measures, which refer generally to quality of life and the scales of Multiple Sclerosis Quality of Life Inventory (MSQLI); life satisfaction, EQ5D, SF-36 • Adverse effects of treatment. • Adverse events leading to withdrawal or lack of efficacy • Expanded Disability Status Scale (EDSS) • MS Functional Composite or its subscales if not reported (MSFC). • Functional improvement • Reduction of care

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			• Mood related outcomes for example validated depression scales and anxiety scales • Changes in sleep quality/sleep related impairments/ sleep disturbance Follow up: • 3 months up to 6 months (less months may be included in view of palliative care subgroup) • If studies only report > 6 months, these may be included and downgraded for indirectness.
E	Intervention	For adults with MS, including people receiving palliative care, what is the clinical and cost effectiveness of pharmacological interventions for mobility?	**Measures of walking ability and upper limb mobility/dexterity for example:** • Walking distance measured by the 6-minute walk test (6MWT) (if not available the 2-minute walk test (2MWT) can be extracted if reported instead) • Walking speed measured by the 25-foot walk (T25FW) (if not available the 10-minute walk test (10MWT) can be extracted if reported instead) • 'Get up and go test' • 12-item Multiple Sclerosis Walking Scale (MSWS-12) • 9 hole peg test (upper limb mobility/dexterity outcome as walk tests, are not applicable to people in wheelchairs). **Health-related quality of life (Validated) for example:** • MS Impact Scale 29 (MSIS-29) • EQ-5D, SF-36, **Adverse events:** • Mortality • Adverse events leading to withdrawal • Urinary tract infections • confusion

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			- seizures - falls - headache - fractures Composite adverse events outcomes will be extracted if none of the above adverse events are reported. **Changes in validated disability or impairment scales assessing for example:** - MS Impact Scale 29 (MSIS-29) - **Motor function** (e.g. Expanded Disability Status Scale (EDSS), the Multiple Sclerosis Functional Composite (MSFC), the Cambridge Multiple Sclerosis Basic Score (CAMBS), the Functional Assessment of Multiple Sclerosis (FAMS), the National Fatigue Index (NFI)) - **Spasticity** (e.g. Modified Ashworth scale, Tardieu Scale, Penn Spasm Frequency Scale (PSFS), Muscle Elastography MS Scale (MEMSs), Fugl Meyer Scale (FMS), Numeric Rating Scale for Spasticity (NRS-S), MS Spasticity Scale-88 (MSSS), Patient-reported Impact of Spasticity Measure (PRISM) - **Fatigue** (e.g. National Fatigue Index (NFI), fatigue Severity Scale (FSS), Modified Fatigue Impact Scale (MFIS)) Follow-up: - At 6 months (if multiple time points are reported, we will only record the closest reported time point up to 6 months) - >6 months - 12 months (data from > 12 months follow up may be included but will be downgraded)
F	Intervention	For adults with MS, including people receiving palliative care, what is the clinical and cost effectiveness of	- Patient-reported outcome measures to assess MS fatigue, including MFIS Fatigue Severity

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		pharmacological interventions for fatigue?	Scale (FSS), National Fatigue Index (NFI), MS-specific FSS (MFSS), Modified Fatigue Impact Scale (MFIS), • Visual Analogue Scale (VAS) • Adverse effects of treatment ○ Adverse events leading to withdrawal ○ Disruption of sleep ○ cardiac events/arrhythmias • Health-related Quality of Life, for example EQ-5D, SF-36, Leeds MS quality of life scale, MS Impact Scale. • Impact on patients/carers. • Cognitive functions, such as memory and concentration • Psychological symptoms assessed by validated and disease-specific scales, questionnaire or similar instruments. • Epworth sleepiness scale **Follow up:** • 3-6 months (minimum of 3 months but can include 1-3 months and downgrade) • >6 months – 1 year (data from >1 year follow up may be included but will be downgraded)
G	Intervention	For adults with MS, including people receiving palliative care, what is the clinical and cost effectiveness of non-pharmacological interventions for fatigue?	• Patient-reported outcome measures to assess MS fatigue, including MFIS Fatigue Severity Scale (FSS), National Fatigue Index (NFI), MS-specific FSS (MFSS), Modified Fatigue Impact Scale (MFIS), and Visual Analogue Scale (VAS) • Health-related Quality of Life, for example EQ-5D, SF-36, Leeds MS quality of life scale, MS Impact Scale.

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			• Impact on carers. • Functional scales that quantify level of disability, such as the Expanded Disability Status Scale (EDSS), the Multiple Sclerosis Functional Composite (MSFC), the Cambridge Multiple Sclerosis Basic Score (CAMBS), or the Functional Assessment of Multiple Sclerosis (FAMS). • Cognitive functions, such as memory and concentration • Psychological symptoms assessed by validated and disease-specific scales, questionnaire or similar instruments. • Adverse effects of treatment for example: ○ Incidence of adverse events ○ Adverse events leading to withdrawal • Outcomes measuring how acceptable to intervention was. These may be measured in terms of how acceptable it was to patients, completion rates, response to follow up, adherence, engagement or disengagement. **Follow up:** • 3-6 months (minimum of 3 months but can include 1-3 months and downgrade) • >6 months – 1 year (can include > 2years for diet, include >12 months but downgrade)
H	Intervention	For adults with MS, including people receiving palliative care, what is the clinical and cost effectiveness of interventions for memory and cognitive problems?	• Objective Measures ○ Cognitive functions, such as memory, attention, executive functions, processing speed, for example, symbol digit modality test (SMDT) • Subjective Measures ○ Health-related Quality of Life, for example EQ-5D, SF-36, Leeds MS quality of life scale, MS Impact Scale.

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			○ Patient-reported outcomes, for example symptoms, activities.(for example Canadian Occupational Performance measure, Cognitive failure questionnaire, perceived deficits questionnaire ○ Self-efficacy/self-management (MS self efficacy scale • Functional Measures ○ Medication management/ adherence to medication ○ Mood ○ Fatigue (MS fatigue scale includes cognition (perhaps include this- if score reported separately?) ○ Activities of daily living (ADL). • Vocational Measures ○ Employment ○ Training ○ Social engagement ○ Relationship satisfaction/ Impact on carers. • Engagement Measures ○ Completion/adherence rates ○ Acceptability ○ Satisfaction Validated measures will be prioritised. If no evidence is available, non-validated may be considered. **Follow up:** • 3-6 months (minimum of 3 months but can include 1-3 months and downgrade) • >6 months – 1 year (data from >1 year follow up may be included but will be downgraded)
I	Intervention	For adults with MS, what is the clinical and cost effectiveness of	• Health-related Quality of Life (validated), for example EQ-5D, SF-

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		pharmacological interventions for ataxia and tremor?	36, Leeds MS quality of life scale, MS Impact Scale. • Ataxia measurement scales: ○ International Cooperative Ataxia Rating Scale (ICARS) • Tremor rating scales (TRS), ○ Fahn ○ SARA ○ 9 hole peg test ○ Archimedean Spiral • Functional scales that quantify level of disability, such as the Expanded Disability Status Scale (EDSS), the Multiple Sclerosis Functional Composite (MSFC), the Cambridge Multiple Sclerosis Basic Score (CAMBS), the Functional Assessment of Multiple Sclerosis (FAMS) or + mobility scales • Adverse effects of treatment: • Withdrawal due to adverse effects (e.g. fatigue) • Patient-reported outcomes, for example symptoms of ataxia and tremor or adverse events. • Impact on carers. Follow-up: • At 6 months (if multiple time points are reported, we will only record the closest reported time point up to 6 months) • >6 months - 12 months (data from >1 year follow up may be included but will be downgraded)
J	Intervention	What is the clinical and cost effectiveness of processes of care, including the role of MS specialist nurses and other healthcare professionals, to improve care coordination and health outcomes in adults with MS?	• Reduction of hospital admissions for: ○ UTI ○ Pressure sores ○ Falls ○ Respiratory infections

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			• Reduction/prevention of unplanned hospital admissions • Reduction in consultant or GP appointments • Treatment adherence • Relapse rates • Improvement in mental health • Patient / carer satisfaction • Functional scales that quantify level of disability, such as the Expanded Disability Status Scale (EDSS), the Multiple Sclerosis Functional Composite (MSFC), the Cambridge Multiple Sclerosis Basic Score (CAMBS), the Functional Assessment of Multiple Sclerosis (FAMS) • Health-related Quality of Life, for example EQ-5D, SF-36, Leeds MS quality of life scale, MS Impact Scale. • Impact on patients and carers (formal and informal). Follow up/Timepoints • 3-12 months (minimum of 3 months but can include 1-3 months and downgrade) • >12 months (data from >12 months follow up may be included but will be downgraded)